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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/745,605	12/22/2000	Gary C. Starling	DB13NP; 30436.43USU1	1201

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	19

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/745,605	STARLING ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2002 and 14 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,27-41 and 43-65* is/are pending in the application.

4a) Of the above claim(s) *6-14,27-41 and 43-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 53-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 12/09/02 (Paper No. 14), is acknowledged.

Claims 1-14, 27-41, 43-65 are pending.

2. Claims 6-14, 27-41 and 43-52 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

3. Claims 1-5 and 53-65 are under examination as they read on an isolated nucleotide sequence of SEQ ID NO:1, encoding a polypeptide of SEQ ID NO 4, vectors, host cells and methods of producing the polypeptide. Furhtermore, the claims read on the elected species, radioisotope.

4. The 37 C.F.R. § 1.131 declaration submitted on 1/14/03 (Paper No. 18) is defective because it contains alterations that are non-initialed and non-dated. Further, two copies of the declaration are found, one for each inventor, one declaration has alterations and the other does not have alteration, it is unclear which one is the correct declaration.

5. The following new grounds of rejections are necessitated by the amendment filed on 12/09/02, paper No. 14.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The recitation of "hybridizes under stringent conditions" in claim 54 is ambiguous. Although the specification discloses on pages 31-32 general parameters for calculating such conditions, it is unclear which conditions are actually claimed.

Applicant argues that pages 31-32 do not merely set forth general parameters, but rather specific conditions.

Examiner suggests that Applicant amend the claims to recite a particular set of hybridization and wash conditions, such as those exemplified on page 31-32 of the specification, to overcome this rejection.

8. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

9. Claims 1-5 and 53-65 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility essentially for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

Applicants argue that the claimed nucleic acid molecules encoding APEX-1, APEX or an agonist thereof may be administered to treat any number of known disorders, including inflammatory, cancer and immune disorders. Applicants further argue that it is established that APEX may be biological target for the treatment of disease states associated with such tissues. Applicants argue that Examiner's reliance on Brenner is misplaced since the present invention is not analogous to Brenner's. Applicants argue that it is not the standard under the Utility Examination or Guidelines or the law to cite various references which purport to teach that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate. Applicants argue that Applicants are not required to show that APEX exhibits functionality to numerous members of a subfamily of which every member is functionally characterized, but rather the Utility Examination Guidelines require that Applicants need only provide one credible assertion of specific and substantial utility to satisfy the utility requirement. Finally, Applicants argue that the Examiner's position appears to be that the biological functionality of APEX must be proven before utility is established.

However, the various utilities recited by the specification which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to APEX-1. Because of this, such utilities are not specific and do not constitute a "well-established" utility. The specification alleges that the claimed protein which is involved with inflammatory, cancer and immune disorders and the disclosed therapeutic uses of the claimed invention center around leukocyte proliferation, differentiation, migration and activation (see Background of the Invention in the specification). However, in the absence of any disclosed relationship between the claimed nucleic acid encoding the polypeptide and any disease or disorder and the lack of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from homology to CD2 subfamily would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing" Brenner, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Applicants argue that the rejection is made based on a scientifically incorrect and legally unsupportable assertion that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate. However, no single effect of the disclosed APEX-1 is ascribed to the claimed protein. Therefore, the original members of the family were not classified based on their biological activity, but rather, by their common structure and the fact that they are cell surface receptors. Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members and is also a cell surface receptor. The members of the family have different biological activities which are related to leukocyte proliferation, differentiation, migration and activation, but there is no evidence that the claimed compounds share any one of those different activities. That is, no activity is known to be common to all members.

The rejection is based on the failure to disclose sufficient properties of the protein and/or polynucleotide to support an inference of utility. The CD2 subfamily to which the polypeptide belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or to which it is administered. Assignment to this family does not support an inference of utility because the members are not known to share a common utility.

None of the utilities which are identified by Applicants, hybridization, treating inflammation, cancer and immune disorder, have been demonstrated to be specific, substantial and credible. One of ordinary skill in the art must understand how to achieve a practical benefit from knowledge of the class, however, there is no practical benefit from use of the claimed invention in hybridization etc. because utility is not specific, substantial and credible. Applicants have not identified a general utility, which is specific, substantial and credible, which applies to the broad class of CD2 subfamily.

10. Claims 1-5 and 53-65 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

Applicants argue that APEX-1 is described in the present specification as a protein encoded by and having the stated sequences, however it is unclear as to why the Examiner does not believe a claim directed to APEX-1 is enabled. Applicants further argue that one of skill in the art would be able to identify variants and polynucleotides, which hybridize to APEX-1 complements.

However, besides the isolated nucleic acid of SEQ ID NO:1 the specification fails to provide how to make any isolated nucleic acid molecule encoding APEX-1. The specification fails to

teach other sequences that encode APEX-1. Furthermore, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to identify the invention. Until the time when those variants and the polynucleotides that hybridize to APEX complement are found, then one skill in the art can make them.

11. Claims 1-5 and 53-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

Applicants argue that the specification describes APEX-1 has a molecule having the amino acid sequence set forth in SEQ ID NO: 4 and encoded by SEQ ID NO:1, however it is unclear as to why the Examiner does not believe that the specification does not provide adequate written description for APEX-1. Applicants further argue that one of skill in the art would be able to recognize variants and polynucleotides, which hybridize to APEX-1 complements.

However, the Examiner notes that the claimed invention which is drawn to a genus may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is no described or art-recognized correlation or relationship between the structure of the invention, the APEX-1 and the asserted utility. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants, wherein the variant has at least 70% polynucleotide sequence identity to the isolated nucleic acid molecule encoding APEX-1. any isolated polynucleotide which hybridizes under stringent conditions to the complement of polynucleotide encoding APEX-1; or any nucleic acid molecule comprising a nucleotide sequence which is complementary to the isolated nucleic acid molecule encoding APEX-1.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 3-5 and 53-57 (previously claims 1, 3-5 and 15-19) are under 35 U.S.C. 102(a) as being anticipated by WO9963088 (Dec 9, 1999) for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

In response to Applicant's argument that the 37 C.F.R. § 1.131 declaration submitted on 1/14/03 (Paper No. 18) overcome the rejection, Examiner notes that the said declaration is defective and therefore was not considered.

14. Claims 53-55 (previously claims 15-17) are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al (GenBand Accetion No. H73135 (1995)) for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

In response to applicant's argument that Hillier *et al* reference is merely set forth an Expressed Sequence Tag which fails to contain a written description or enabaling disclosure of any such polynucleotides or nucleic acid molecules, products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 56 and 58 (previously claims 1, 18 and 20) are rejected under 35 U.S.C. 103(a) as being unpatentable over WO996308 in view of Adams el al (biochemistry of the nucleic acids))) for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

In response to Applicant's argument that the 37 C.F.R. § 1.131 declaration submitted on 1/14/03 (Paper No. 18) overcome the rejection, Examiner notes that the said declaration is defective and therefore was not considered.

17. Claims 59-60 (previously claims 21-22) are rejected under 35 U.S.C. 103(a) as being unpatentable over WO996308 in view of U.S. Patent No. 6,134,002)) for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

In response to Applicant's argument that the 37 C.F.R. § 1.131 declaration submitted on 1/14/03 (Paper No. 18) overcome the rejection, Examiner notes that the said declaration is defective and therefore was not considered.

18. Claims 61-64 and 65 (previously claims 23-26 and 42) are rejected under 35 U.S.C. 103(a) as being unpatentable over WO996308 in view of Darnell et al)) for the same reasons set forth in the previous Office Action, paper No. 12, mailed 6/05/02.

Applicants' arguments, filed 12-09-02, Paper No. 14 have been fully considered but not persuasive.

In response to Applicant's argument that the 37 C.F.R. § 1.131 declaration submitted on 1/14/03 (Paper No. 18) overcome the rejection, Examiner notes that the said declaration is defective and therefore was not considered.

19. No claim allowed

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
February 24, 2003

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